Patent Application No. 10/030,452 Masayuki YABUTA et al. September 13, 2006 Attorney Docket No. 58777.000008

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1 and 2 (Canceled)

Claim 3 (Previously Presented): The method as defined in Claim 9 or 10 wherein the host cell is a prokaryotic cell or an eukaryotic cell.

Claim 4 (Previously Presented): The method as defined in Claim 3 wherein the host cell is a microorganism.

Claim 5 (Previously Presented): The method as defined in Claim 4 wherein the microorganism is *Escherichia coli*.

Claim 6 (Previously Presented): The method as defined in any one of Claims 9 and 10 wherein the molecular weight of the polypeptide comprising a serine residue is about 1000 to 20000.

Claim 7 (Canceled)

Claim 8 (Previously Presented): The method as defined in any one of Claims 9 and 10 wherein the atrial natriuretic peptide is human atrial natriuretic peptide.

Claim 9 (Previously Presented): A method for reducing formation of a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue, comprising:

(i) culturing, in a medium, transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;

3

Patent Application No. 10/030,452 Masayuki YABUTA et al. September 13, 2006 Attorney Docket No. 58777.000008

- (ii) adding to said medium at least one of histidine, methionine or glycine in an amount effective to reduce said byproduct formation; and
- (iii) reducing the formation of said byproduct polypeptide.

Claim 10 (Previously Presented): A method for producing a polypeptide comprising a serine residue comprising:

- (i) culturing, in a medium, transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;
- (ii) adding at least one of histidine, methionine or glycine to the medium in an amount effective to reduce said byproduct formation; and
- (iii) reducing the formation of said byproduct polypeptide.

Claim 11 (Previously Presented): A culture medium comprising:

- (i) transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;
- (ii) at least one of histidine, methionine or glycine added to the medium in an amount effective to reduce formation of a byproduct polypeptide comprising O-acetylserine residue in place of a serine residue; and
- (iii) a reduced formation of said byproduct polypeptide as compared with a control medium with no histidine, methionine or glycine added.

Claim 12 (Previously Presented): The culture medium of claim 11 wherein the formation of said byproduct polypeptide is reduced in an amount greater than or equal to 50% as compared with said control medium.

Claim 13 (New): The culture medium of claim 11 wherein the amount of methionine effective to reduce formation of a byproduct polypeptide comprising O-acetylserine residue in place of a serine residue is 3 g/L.

Patent Application No. 10/030,452 Masayuki YABUTA et al. September 13, 2006 Attorney Docket No. 58777,000008

Claim 14 (New): The method of any one of claims 9 or 10 wherein the amount of methionine effective to reduce formation of a byproduct polypeptide comprising O-acetylserine residue in place of a serine residue is 3 g/L.

Claim 15 (New): The culture medium of claim 11 comprising methionine and at least one of histidine or glycine added to the medium in an amount effective to reduce formation of a byproduct polypeptide comprising O-acetylserine residue in place of a serine residue

Claim 16 (New): The method of any one of claims 9 or 10 comprising adding methionine and at least one of histidine or glycine in an amount effective to reduce formation of said byproduct.

Claim 17 (New): A method for reducing formation of a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue, comprising:

- (i) culturing, in a medium, transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;
- (ii) adding to said medium at least one of histidine or glycine in an amount effective to reduce said byproduct formation; and
- (iii) reducing the formation of said byproduct polypeptide.

Claim 18 (New): A method for producing a polypeptide comprising a serine residue comprising:

- (i) culturing, in a medium, transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;
- (ii) adding at least one of histidine or glycine to the medium in an amount effective to reduce said byproduct formation; and
- (iii) reducing the formation of said byproduct polypeptide.

Patent Application No. 10/030,452 Masayuki YABUTA et al. September 13, 2006 Attorney Docket No. 58777.000008

Claim 19 (New): A culture medium comprising:

- (i) transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue;
- (ii) at least one of histidine or glycine added to the medium in an amount effective to reduce formation of a byproduct polypeptide comprising O-acetylserine residue in place of a serine residue; and
- (iii) a reduced formation of said byproduct polypeptide as compared with a control medium with no histidine or glycine added.

Claim 20 (New): The culture medium of claim 19 wherein the formation of said byproduct polypeptide is reduced in an amount greater than or equal to 50% as compared with said control medium.